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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,176	07/12/2004	George A. Doherty	21014YP	7849

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
4173	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,176	DOHERTY ET AL.	
	Examiner	Art Unit	
	Samira Jean-Louis	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *12,15-18, 20-45, and 60-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-14,19 and 46-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sheets (2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-61 are pending in the application. However, claims 1-11,13-14,19 and 46-59 are being examined on the merits herein due to a restriction/election requirement.

Applicant's election with traverse to various species in the reply filed on 09/25/07 is acknowledged. The traversal is on the ground(s) that the groups are properly linked to form a single general inventive concept. This is not found persuasive because the claims recited in the instant application recite a multiplicity of groups that do not form a single general inventive concept and lack the same special technical features. Particularly, group I of the instant application is drawn to a method of treating an immunoregulatory abnormality comprising administering to said patient a compound which is a selective agonist of the S1P1/Edg1 receptor over the S1P3/Edg3 while group III of the of the instant application is drawn to a method of identifying a candidate compound, which is a selective agonist of the S1P1/Edg1 receptor over S1P3/Edg3. As a result, these groups are patentably distinct and fully capable of supporting separate patents. Furthermore, given that the claims recite such a multiplicity of compounds that are contrastingly different in structure and chemical properties, a search would indeed be unduly extensive and burdensome given that a search for these species would consist of searching multiple databases for various references and literature searches.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 12,15-18, 20-45, and 60-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Objections

The abstract of the disclosure is objected to because it contains legal phraseology such as "comprising" in lines 2 and 8 or "said compound" or "said immunoregulatory abnormality" or "said patient" or "said respiratory disease" in lines 3-4, and 8-9. Correction is required. See MPEP § 608.01(b).

Written Description Rejection (Insufficient Disclosure)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11,13-14,19 and 46-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated by the court in Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), regarding the written description requirement:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

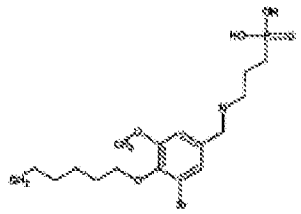
In this instant application, applicant did not specifically described what an immunoregulatory abnormality entails in the claim(s) (i.e. claim 1) or in the specification (see specification pg. 4, line 16, pg. 5, line 2, etc...). For example, ankylosing spondylitis involves the immune system and yet was not disclosed by applicant as an immunoregulatory abnormality rendering it impossible for one skill in the art to envisage what is truly meant by immunoregulatory abnormality. Consequently, due to this lack of written description, the exact interpretation of immunoregulatory abnormality being claimed by applicant cannot be fully ascertained.

Scope of Enablement Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11,13-14,19 and 46-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for example 77,



in the treatment of lymphopenia, does not reasonably provide enablement for all of the disclosed compounds in the specification (see pages 13-27) or the treatment of all of the disclosed examples of immunoregulatory abnormalities. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is a selective agonist of the S1P1/Edg1 receptor over S1P3/Edg3 receptor in an amount effective for treating said immunoregulatory abnormality. The instant specification fails to provide information that would allow the skilled artisan to practice the treatment of all diseases associated with immunoregulatory abnormality.

[In re Sichert, 196 USPQ 209 (CCPA 1977)]

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not

The invention relates to a method of treating immunoregulatory abnormality in a mammalian patient comprising administering to said patient a compound that is a selective agonist of the S1P1/Edg1 receptor over S1P3/Edg3 receptor while claim 46 is drawn to a method of treating a respiratory disease or condition utilizing the same aforementioned compound. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites A. Raza who describes the state of the art in the treatment of rheumatoid arthritis (an example of immunoregulatory abnormality), as palliative care given that no cures are currently in existence.

2. The breadth of the claims

Since the instant specification provides no limiting definition of the term "immunoregulatory abnormality", the examiner will adopt the broadest reasonable interpretation for same. Webster's Ninth New Collegiate Dictionary defines "abnormality" as "aberrant", i.e., to control the aberrant deficiencies of the immune system.

The claims are thus very broad insofar as they recite the "treatment of immunoregulatory abnormalities". While such "treatment" might theoretically be possible for some immunoregulatory abnormalities, as a practical matter it is nearly impossible to achieve a treatment for all possible immunoregulatory abnormalities with the same compound.

"experimentation".

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for all compounds and all disease subtypes. No reasonably specific guidance is provided concerning useful therapeutic protocols for all of the disclosed compounds, other than example 77. The latter is corroborated by the working examples on page 163.

[The instant disclosure provides no evidence to suggest that this unique activity can be extrapolated to rheumatoid arthritis, for example, having unrelated mechanisms of resistance, and thus does not meet the "how to use" prong of 35 USC 112, first paragraph with regard thereto.]

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used for the treatments of all immunoregulatory abnormalities as inferred by the claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no

assurance of success.

Claim Rejections - 35 USC § 112 (Lack of Antecedent Basis)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-11,13-14,19 and 46-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11,13-14,19 and 46-59 recite the limitation "the ^{35}S-GTPγS" in line 10 of claims 1 and 6, line 28 of claims 46 and 51, and line 11 of claim 59. There is insufficient antecedent basis for this limitation in the claim.

Provisional Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 34 of copending Application No. 10500895 (hereinafter Bugianesi US Patent Application No. '895). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound in accordance with claim 1 (i.e. selective agonist for the S1P1 receptor over S1P3 receptor) in an amount that is effective for treating said immunoregulatory abnormality. The claimed invention and co-

pending application Bugianesi '895 are rendered obvious over another as the claimed invention teaches a broad genus of compounds whereas Bugianesi '895 teaches a subgenus of the aforementioned compounds in the treatment of immunoregulatory abnormality. Thus, the aforementioned claim of the instant application is substantially overlapping in scope as discussed hereinabove and is prima facie obvious over the cited claims of corresponding application No. 10500895.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19 of copending Application No. 10554665 (hereinafter Colandrea US Patent Application No. '665). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound in accordance with claim 1 (i.e. selective agonist for the S1P1 receptor over S1P3 receptor) in an amount that is effective for treating said immunoregulatory abnormality. The claimed invention and co-pending application Colandrea '665 are rendered obvious over another as the claimed invention teaches a broad genus of compounds whereas Colandrea '665 teaches a subgenus of the aforementioned compounds in the treatment of immunoregulatory

abnormality. Thus, the aforementioned claim of the instant application is substantially overlapping in scope as discussed hereinabove and is prima facie obvious over the cited claims of corresponding application No. 10554665.

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 14 of copending Application No. 10571334 (hereinafter Doherty US Patent Application No. '334). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound in accordance with claim 1 (i.e. selective agonist for the S1P1 receptor over S1P3 receptor) in an amount that is effective for treating said immunoregulatory abnormality. The claimed invention and co-pending application Doherty '334 are rendered obvious over another as the claimed invention teaches a broad genus of compounds whereas Doherty '334 teaches a subgenus of the aforementioned compounds in the treatment of immunoregulatory abnormality. Thus, the aforementioned claim of the instant application is substantially overlapping in scope as discussed hereinabove and is prima facie obvious over the cited claims of corresponding application No. 10571334.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SJL

11/14/2007

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614